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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,271	09/06/2005	Andrew Simon Goldsborough	CGS-102	5614

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EXAMINER	
POHNERT, STEVEN C	
ART UNIT	**PAPER NUMBER**
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/523,271	GOLDSBOROUGH, ANDREW SIMON	
	Examiner	Art Unit	
	Steven C. Pohnert	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *26-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/ are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/3/2006, 8/31/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-25, in the reply filed on 11/1/2007 is acknowledged. The traversal is on the ground(s) that Goldsborough does not specifically teach the use of a primary amine for deprotection, however, the kit components of the kit were known and lack a special technical feature over the prior art. The intended use of the primary amine as a deprotection agent is not a special technical feature of the kit and thus does not represent a distinguishing feature over Goldsborough. Goldsborough teaches a kit comprising a reaction system, a separation system, and aniline (a primary amine). Thus the kit does lack a special technical feature over the prior art and thus lacks unity of invention.

The requirement is still deemed proper and is therefore made FINAL.

1. Claims 26-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 11/1/2007.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim15 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 recites, "wherein the chelator is a salt of ammonia or tetra-alkylammonium." It is unclear if the claim is drawn to an ammonia salt or tetra-alkylammonium or ammonia salt or tetra-alkylammonium salt.

Claim 22 recites the method acccrding to claim 9, wherein the deprotection step occurs between step (i) and step (ii). However, neither claim 9, nor claim 1 from which it depends have a step (i) or (ii). Thus it is unclear where the deprotection step occurs.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-12, 13, 15, 16, and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goldsborough (WO00/75302 , published December 14, 2000) in view of Greene et al (Protective groups in organic synthesis, Third edition (1999) pages 160-161).

With regards to claim 1, Goldsborough et al teaches a method of treating a sample so that the 2'-OH of RNA is modified and isolating the nucleic acid following modification (see page 3, 1st paragraph). Goldsborough teaches the method provides for obtaining intact full-length copies of RNA isolated from cellular sources or extracellular fluids. Goldsborough teaches obtaining a biological sample (page 4, 2nd full paragraph). Goldsborough teaches, "the RNA can be deprotected by cleavage of the modifying group with 50% ammonia treatment, 10-40mM KCN (final concentration)

in 95% EtOH, K2C03 in aqueous methanol or other conditions which are known to lead to the cleavage of the ester linkage (see Protective Groups In Organic Chemistry, 2nd edition, Ed. T. W. Greene, Wiley- Interscience)" (see page 41, 1st paragraph). Goldsborough teaches the RNA is then collected and purified further if required (see page 41, 1st paragraph). Goldsborough thus teaches a method of collecting a biological sample, treating the sample to protect the 2'OH, isolating the treated sample, and deprotecting.

With regards to claim 2, Goldsborough teaches the RNA is isolated from virus, bacteria (cells), blood or body fluids (see page 4, 2nd and 3rd paragraphs and page 24, last full paragraph).

With regards to claim 3, Goldborough teaches, "RNA can be derived from a biological material such as bacteria, viruses such as those causing infection in humans, animals or plants, viroids, or cells such as fungal, animal and plant cells." Goldsborough thus teaches the biological fluid comprises a pathogen.

With regards to claims 4 and 5, Goldborough teach the nucleic acid is single stranded RNA and the 2'-OH is modified (see abstract).

With regards to claim 6, Goldsborough teaches an organic solvent is used in the reaction medium (see page 13). Goldsborough thus teaches the step (b) takes plase in an organic solvent.

With regards to claim 7, Goldsborough teaches the use of dimethyl sulphoxide (see page 13), which has a flash point above 37°C.

The specification set forth no limiting definition of homogeneous.

With regards to claim 8, Goldsborough teaches the use of DMSO. DMSO is capable of forming a homogenous solution with human blood when mixed at a 5:1 ratio.

With regards to claim 10, Goldsborough teaches attaching to BCPB beads and then washing the beads with ethanol and water (see page 47). Goldsborough teaches the RNA is released from the first solid (see page 47, last 3 lines). Goldsborough thus teaches a method of binding a nucleic acid to a solid phase, optionally washing the solid phase to remove contaminants, and optionally eluting for the solid phase.

With regards to claim 11, Goldsborough teaches the use of magnetic or paramagnetic particles with a polymeric linear, globular or cross-linked molecule(see page 23, first full paragraph).

With regards to claim 12, Goldsborough teaches his method allows modification of the phosphate group to the beads or particles of the invention. Thus Goldsborough teaches the solid phase contains a metal or metal ion capable of coordinating with phosphate. Goldsborough teaches use of silicon beads.

Claim 15 is indefinite in that it is unclear if the claim requires an ammonia salt, a tetra-alkylammonium salt or ammonia or tetra-alkylammonium. The claim is thus being give its broadest reasonable interpretation that it requires ammonia or tetra-alkylammonium.

With regards to claim 13 and 15, Goldsborough teaches the release of RNA using ammonia (see page 41, line 12).

With regards to claim 16, Goldsborough teaches the use of Centricon-50 columns to separate the salts (see page 43, 1st full paragraph). Goldsborough thus teaches removing chelator by filtration.

Claim 22 is indefinite as it is directed to steps that are not present in claim 9, or 1 from which claim 1 depends. Claim 22 is thus being given its broadest reasonable interpretation that there is a deprotection step.

With regards to claim 22, Goldsborough teaches deprotection.

With regards to claim 23, Goldsborough teaches the use of silica beads (see page 36).

With regards to claim 24, Goldsborough teach binding of BMV RNA to BCPB beads and subsequent hybridization of a radio labeled BMV RNA probe to the BMV-RNA-bead complex (see page 48). Thus Goldsborough teaches isolation of the radio labeled BMV-RNA by the complementary BMV-RNA-bead complex.

With regards to claim 25, Goldsborough teaches Binding of 512 ng of BV RNA to BCPB beads, subsequent reaction with a second modifier, such as biotin, release (deprotection) of the RNA from the beads before, attachment to streptavidin beads by the biotin (see page 47). Thus Goldsborough teaches the RNA is isolated and subject to a deprotecting step (release from BCPB beads) before attachment to a solid phase (streptaviding beads).

Goldsborough does not teach a method of stabilizing and isolating a nucleic acid from a sample, wherein the nucleic acid is deprotected by treatment with a primary amine..

However, Greene et al teaches the cleavage of ester linkages by use of $HSCH_2CH_2NH_2$ or $H_2NCH_2CH_2NH_2$ (ethylenediamine) (see page 161, #1) (claim 9).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the primary amine or ethylenediamine ester cleavage method of Greene et al as a reactant to remove the protecting group in the method of Goldsborough. The artisan would be motivated to use ethylenediamine because it is specifically taught by Greene. The ordinary artisan would be motivated because Goldsborough suggests the use of any ester cleavage reagent and specifically directs the artisan to the work of Greene. The artisan would thus be substituting one know method of ester cleavage reagent with another know method of ester cleavage and thus would have a probability of success.

6. Claim 14 rejected under 35 U.S.C. 103(a) as being unpatentable over Goldsborough (WO00/75302 , published December 14, 2000) in view of Greene et al (Protective groups in organic synthesis, Third edition (1999) pages 160-161) as applied to claims 1-13, 15, 16 and 22-25 above, and further in view of Padhye (US Patent 5,808,041, issued September 15, 1998).

Goldsborough and Green do not teach the elution of nucleic acid using EGTA with a pH above 9.

However, Padhye et al teaches elution in sample containing EDTA or EGTA (see column 6, lines 26-29). Padhye further teaches elution in of nucleic acids in buffers with a pH about 8.5 (see column 9, lines 22-24). A pH of about 8.5 is about 9.

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the EGTA solution of pH 9 in the method of Goldsbrough using silica beads to release the modified RNA. The skilled artisan would be motivated to substitute the method of elution taught by Goldsborough with the EGTA solution of Padhye, because Padhye demonstrates that EGTA solutions are known in the art to elute nucleic acids from silica beads.

7. Claims 17-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goldsborough (WO00/75302 , published December 14, 2000) in view of Greene et al (Protective groups in organic synthesis, Third edition (1999) pages 160-161) as applied to claim1-13, 15, 16 and 22-25 above, and further in view of Michelsen et al (US Patent 6,355,792, Issue March 12, 2002).

The teachings of Goldsborough in view of Greene are set forth in paragraph 5.

Goldsborough et al does not teach the use of hydroxapatite as a solid phase (claim 17), wherein the hydroxyapatite is prewashed with a phosphate containing compound (claim 18), washing with a primary amine (claims 19 and 20), or wherein deprotection comprises step (ii) (claim 21).

However, Michelsen teaches a method of isolating nucleic acids by their binding to silica gel or hydroxypatite (see abstract and column 2, lines 35-36). Michelsen teaches washing the resins bound with the nucleic acids with Tris-HCl (see column 4, line 42). Michelsen teaches eluting with a Tris contatining buffer (see column 4, line 42). Tris is an amine and a primary amine. Michelsen further teaches the hydoxypatite is treated with DNA/RNA mixture before washing. RNA and DNA are phosphate

containing compounds. Thus Michelsen teaches pretreatment of hydroxypatite with a phosphate containing compounds.

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to substitute the hydroxypatite of Michelsen for the silica beads of Goldsborough with a reasonable expectation of success. The ordinary artisan would have substitute hydroxpatite for the silica of Goldsborough because Michelsen teaches the use of either silica gel or hydroxypatite for binding of nucleic acid were known and accepted methods methods of nucleic acid isolation at the time of the invention. Thus the substitution of hydroxypatite for silica beads would merely be a substitution of one art accepted nucleic acid binding agent for another DNA binding agent. The artisan would have a high probability of success as the substitution is an art accepted alternative.

Summary

No claims are allowed over prior art cited.

Conclusions

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven C. Pohnert whose telephone number is 571-272-3803. The examiner can normally be reached on Monday-Friday 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Steven Pohnert

RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER